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DATE: Monday, February 07, 2005

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		<i>DB=USPT; PLUR=YES; OP=AND</i>	
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END OF SEARCH HISTORY

## Search Results - Record(s) 1 through 9 of 9 returned.

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- ☐ 1. 20040253673. 05 Dec 03. 16 Dec 04. Recombinant botulinum toxins with a soluble C-terminal portion. Williams, James A.. 435/69.1; 435/252.33 435/254.2 435/320.1 435/348 530/350 536/23.7 C07K014/33 C07H021/04 C12N001/21.
- 
- ☐ 2. 20040235118. 04 Dec 03. 25 Nov 04. Portions of soluble recombinant botulinum toxins. Williams, James A.. 435/69.7; C12P021/04.
- 
- ☐ 3. 20040219637. 05 Dec 03. 04 Nov 04. Soluble recombinant botulinum toxins having a C-terminal portion of a heavy chain, a N-terminal portion of a heavy chain and a light chain. Williams, James A.. 435/69.3; 435/252.33 435/254.2 435/320.1 435/348 C12P021/02 C12N001/18 C12N005/06.
- 
- ☐ 4. 20040142455. 05 Dec 03. 22 Jul 04. Recombinant botulinum toxins having a soluble C-terminal portion of a heavy chain, an N-terminal portion of a heavy chain and a light chain. Williams, James A.. 435/252.33; 435/254.2 435/320.1 435/348 435/69.3 530/350 536/23.7 C12P021/02 C12N001/21 C12N001/18 C12N005/06.
- 
- ☐ 5. 20040115215. 05 Dec 03. 17 Jun 04. Recombinant botulinum toxins with a soluble C-terminal portion, an N-terminal portion and a light chain. Williams, James A.. 424/184.1; A61K039/395 A61K039/00 A61K039/38.
- 
- ☐ 6. 20030219457. 15 Oct 02. 27 Nov 03. Soluble recombinant botulinum toxins. Williams, James A.. 424/199.1; 424/186.1 424/234.1 435/6 C12Q001/68 A61K039/12 A61K039/02.
- 
- ☐ 7. 20030215468. 30 Jan 03. 20 Nov 03. Soluble recombinant botulinum toxin proteins. Williams, James A., et al. 424/239.1; 435/252.3 435/70.21 530/388.4 A61K039/08 C12P021/04 C12N001/21 C07K016/12.
- 
- ☐ 8. 20030118547. 14 Nov 02. 26 Jun 03. Composition for intestinal delivery. Vandenberg, Grant William. 424/85.4; 424/130.1 424/85.2 424/93.2 514/169 514/2 514/54 514/560 A61K048/00 A61K038/21 A61K031/715 A61K038/24 A61K038/20 A61K031/573 A61K031/20 A61K031/56 A61K039/395.
- 
- ☐ 9. 20030108597. 13 Aug 02. 12 Jun 03. Application of lipid vehicles and use for drug delivery. Chancellor, Michael B., et al. 424/450; 424/143.1 424/239.1 424/760 514/44 514/625 A61K048/00 A61K039/395 A61K009/127 A61K035/78 A61K031/16 A61K039/08.
-

DERWENT-ACC-NO: 1998-230234

DERWENT-WEEK: 200482

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TITLE: Host cell containing recombinant expression vector encoding Clostridium botulinum type B or E toxin - useful to treat humans and other animals at risk of intoxication with clostridial toxin

INVENTOR: THALLEY, B S; WILLIAMS, J A

PATENT-ASSIGNEE: OPHIDIAN PHARM INC (OPHIN), ALLERGAN BOTOX LTD (ALLR),  
ALLERGAN INC (ALLR), ALLERGAN SALES INC (ALLR)

PRIORITY-DATA: 1996US-0704159 (August 28, 1996), 1995US-0405496 (March 16, 1995), 2003US-0354774 (January 30, 2003), 2002US-0271012 (October 15, 2002), 2003US-0729122 (December 5, 2003), 2003US-0729039 (December 5, 2003), 2003US-0729527 (December 5, 2003), 2003US-0727898 (December 4, 2003), 2003US-0728696 (December 5, 2003)

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## PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
<input type="checkbox"/> <u>US 20040253673 A1</u>	December 16, 2004		000	C07K014/33
<input type="checkbox"/> <u>WO 9808540 A1</u>	March 5, 1998	E	427	A61K039/00
<input type="checkbox"/> <u>AU 9742450 A</u>	March 19, 1998		000	
<input type="checkbox"/> <u>EP 1105153 A1</u>	June 13, 2001	E	000	A61K039/00
<input type="checkbox"/> <u>US 20030215468 A1</u>	November 20, 2003		000	A61K039/08
<input type="checkbox"/> <u>US 20030219457 A1</u>	November 27, 2003		000	C12Q001/68
<input type="checkbox"/> <u>US 20040115215 A1</u>	June 17, 2004		000	A61K039/395
<input type="checkbox"/> <u>US 20040142455 A1</u>	July 22, 2004		000	C12P021/02
<input type="checkbox"/> <u>US 20040219637 A1</u>	November 4, 2004		000	C12P021/02
<input type="checkbox"/> <u>US 20040235118 A1</u>	November 25, 2004		000	C12P021/04

DESIGNATED-STATES: AU CA JP AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE  
 AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

## APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	DESCRIPTOR
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US20040253673A1	October 15, 2002	2002US-0271012	Div ex
US20040253673A1	December 5, 2003	2003US-0728696	
US20040253673A1		US 5919665	CIP of
WO 9808540A1	August 28, 1997	1997WO-US15394	

AU 9742450A	August 28, 1997	1997AU-0042450	
AU 9742450A		WO 9808540	Based on
EP 1105153A1	August 28, 1997	1997EP-0940746	
EP 1105153A1	August 28, 1997	1997WO-US15394	
EP 1105153A1		WO 9808540	Based on
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US20040142455A1	August 28, 1996	1996US-0704159	Cont of
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US20040235118A1	March 16, 1995	1995US-0405496	CIP of
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US20040235118A1	January 30, 2003	2003US-0354774	Div ex
US20040235118A1	December 4, 2003	2003US-0727898	
US20040235118A1		US 5919665	CIP of

INT-CL (IPC): A61 K 38/08; A61 K 39/00; A61 K 39/02; A61 K 39/08; A61 K 39/12; A61 K 39/38; A61 K 39/395; C07 H 21/04; C07 K 14/33; C07 K 16/00; C07 K 16/12; C12 N 1/18; C12 N 1/21; C12 N 5/06; C12 N 15/00; C12 N 15/09; C12 N 15/63; C12 N 15/70; C12 N 15/74; C12 P 21/02; C12 P 21/04; C12 P 21/06; C12 P 21/08; C12 Q 1/68

RELATED-ACC-NO: 1994-217494;1994-271898 ;1994-341765 ;1996-230603

ABSTRACTED-PUB-NO: WO 9808540A

BASIC-ABSTRACT:

Host cell, containing a recombinant expression vector, which encodes a protein comprising at least a portion of a Clostridium botulinum type B or E toxin, is claimed. Also claimed are: (1) a host cell containing a recombinant expression vector, which encodes a fusion protein comprising a non-toxin protein sequence, preferably comprising a poly-histidine tract, and at least a portion, preferably comprising the receptor binding domain, of a C. botulinum type B or E toxin; and (2) a vaccine, preferably endotoxin free, comprising the fusion protein of (1), and preferably further comprising a fusion protein comprising a non-toxin protein sequence and at least a portion of C. botulinum type A toxin.

USE - An antigen comprising the fusion protein can be used to generate a novel antibody (Ab) directed against a C. botulinum toxin (claimed). The vaccine and the Ab can be used to treat humans and other animals at risk of intoxication with clostridial toxin, while the Ab or the protein can also be used for the detection of bacterial toxins.

ABSTRACTED-PUB-NO: WO 9808540A

EQUIVALENT-ABSTRACTS:

CHOSEN-DRAWING: Dwg.0/40

DERWENT-CLASS: B04 D16

CPI-CODES: B04-E08; B04-G01; B04-N0300E; B12-K04A4; B14-A01; B14-S11B; D05-H07; D05-H11; D05-H14A1; D05-H17C;

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## P10845

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[\[Features\]](#) [\[Sequence\]](#) [\[Tools\]](#)

*Note: most headings are clickable, even if they don't appear as links. They link to the user manual or other documents.*

### Entry information

Entry name **BXA1\_CLOBO**  
Primary accession number **P10845**  
Secondary accession numbers **P01561 P18639**  
Entered in Swiss-Prot in **Release 11, July 1989**  
Sequence was last modified in **Release 26, July 1993**  
Annotations were last modified in **Release 46, February 2005**

### Name and origin of the protein

Protein name **Botulinum neurotoxin type A [Precursor]**  
Synonyms **EC 3.4.24.69**  
**BoNT/A**  
**Bontoxilysin A**  
**BOTOX**

Contains **Botulinum neurotoxin A, light-chain**  
**Botulinum neurotoxin A, heavy-chain**

Gene name **Name: botA**

Synonyms: atx, bna

From **Clostridium botulinum [TaxID: 1491]**

Taxonomy **Bacteria; Firmicutes; Clostridia; Clostridiales; Clostridiaceae; Clostridium.**

### References

- [1] NUCLEOTIDE SEQUENCE.  
**STRAIN=Type A / NCTC 2916;**  
**MEDLINE=90235864;PubMed=2185020 [NCBI, ExPASy, EBI, Israel, Japan]**  
**Thompson D.E., Brehm J.K., Oultram J.D., Swinfield T.-J., Shone C.C., Atkinson T., Melling J., Minton N.P.;**  
**"The complete amino acid sequence of the Clostridium botulinum type A neurotoxin, deduced by nucleotide sequence analysis of the encoding gene.";**  
**Eur. J. Biochem. 189:73-81(1990).**
- [2] NUCLEOTIDE SEQUENCE.

**STRAIN**=Type A / 62A;

**MEDLINE**=90264400;PubMed=2160960 [NCBI, ExPASy, EBI, Israel, Japan]

Binz B., Kuarzono H., Wille M., Frevent J., Wernars K., Niemann H.;

"The complete sequence of botulinum neurotoxin type A and comparison with other clostridial neurotoxins.";

J. Biol. Chem. 265:9153-9158(1990).

[3] **NUCLEOTIDE SEQUENCE OF 1-65.**

**STRAIN**=Type A / 62A;

**MEDLINE**=97016817;PubMed=8863443 [NCBI, ExPASy, EBI, Israel, Japan]

East A.K., Bhandari M., Stacey J.M., Campbell K.D., Collins M.D.;

"Organization and phylogenetic interrelationships of genes encoding components of the botulinum toxin complex in proteolytic *Clostridium botulinum* types A, B, and F: evidence of chimeric sequences in the gene encoding the nontoxic nonhemagglutinin component.";

Int. J. Syst. Bacteriol. 46:1105-1112(1996).

[4] **NUCLEOTIDE SEQUENCE OF 1-34.**

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**MEDLINE**=89350959;PubMed=2669749 [NCBI, ExPASy, EBI, Israel, Japan]

Betley M.J., Somers E., Dasgupta B.R.;

"Characterization of botulinum type A neurotoxin gene: delineation of the N-terminal encoding region.";

Biochem. Biophys. Res. Commun. 162:1388-1395(1989).

[5] **NUCLEOTIDE SEQUENCE OF 1-18.**

**STRAIN**=Type A / NIH;

DOI=10.1016/0014-5793(95)01241-5;MEDLINE=96096783;PubMed=8521962 [NCBI, ExPASy, EBI, Israel, Japan]

Fujita R., Fujinaga Y., Inoue K., Nakajima H., Kumon H., Oguma K.;

"Molecular characterization of two forms of nontoxic-nonhemagglutinin components of *Clostridium botulinum* type A progenitor toxins.";

FEBS Lett. 376:41-44(1995).

[6] **PROTEIN SEQUENCE OF 1-16.**

**MEDLINE**=84178501;PubMed=6370252 [NCBI, ExPASy, EBI, Israel, Japan]

Schmidt J.J., Sartymoorthy V., Dasgupta B.R.;

"Partial amino acid sequence of the heavy and light chains of botulinum neurotoxin type A.";

Biochem. Biophys. Res. Commun. 119:900-904(1984).

[7] **PROTEIN SEQUENCE OF 1-46.**

Dasgupta B.R., Foley J., Niece R.;

"Partial sequence of the light chain of botulinum neurotoxin type A.";

Biochemistry 26:4162-4162(1987).

[8] **PROTEIN SEQUENCE OF 1-5 AND 444-456.**

DOI=10.1016/0300-9084(90)90048-L;MEDLINE=91120847;PubMed=2126206 [NCBI, ExPASy, EBI, Israel, Japan]

Dasgupta B.R., Dekleva M.L.;

"Botulinum neurotoxin type A: sequence of amino acids at the N-terminus and around the nicking site.";

Biochimie 72:661-664(1990).

[9] **PROTEIN SEQUENCE OF 448-464 AND 872-895.**

**MEDLINE**=89024662;PubMed=3178218 [NCBI, ExPASy, EBI, Israel, Japan]

Sathymoorthy V., Dasgupta B.R., Foley J., Niece R.L.;

"Botulinum neurotoxin type A: cleavage of the heavy chain into two halves and their partial sequences.";

Arch. Biochem. Biophys. 266:142-151(1988).

[10] PROTEIN SEQUENCE OF 448-482.

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Shone C.C., Hambleton P., Melling J.;

"Inactivation of Clostridium botulinum type A neurotoxin by trypsin and purification of two tryptic fragments. Proteolytic action near the COOH-terminus of the heavy subunit destroys toxin-binding activity.";

Eur. J. Biochem. 151:75-82(1985).

[11] PROTEIN SEQUENCE OF 866-879 AND 1147-1218.

PubMed=8397793 [NCBI, ExPASy, EBI, Israel, Japan]

Gimenez J.A., DasGupta B.R.;

"Botulinum type A neurotoxin digested with pepsin yields 132, 97, 72, 45, 42, and 18 kD fragments.";

J. Protein Chem. 12:351-363(1993).

[12] IDENTIFICATION OF SUBSTRATE.

DOI=10.1016/0014-5793(93)80448-4;MEDLINE=94063091;PubMed=8243676 [NCBI, ExPASy, EBI, Israel, Japan]

Schiavo G., Santtuci A., Dasgupta B.R., Mehta P.P., Jontes J., Benfenati F., Wilson M.C., Montecucco C.;

"Botulinum neurotoxins serotypes A and E cleave SNAP-25 at distinct COOH-terminal peptide bonds.";

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[13] IDENTIFICATION OF SUBSTRATE.

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Binz T., Blasi J., Yamasaki S., Baumeister A., Link E., Suedhof T.C., Jahn R., Niemann H.;

"Proteolysis of SNAP-25 by types E and A botulinal neurotoxins.";

J. Biol. Chem. 269:1617-1620(1994).

[14] MUTAGENESIS OF GLU-261; PHE-265 AND TYR-365.

DOI=10.1006/bbrc.2001.5911;MEDLINE=21556941;PubMed=11700044 [NCBI, ExPASy, EBI, Israel, Japan]

Rigoni M., Caccin P., Johnson E.A., Montecucco C., Rossetto O.;

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[15] X-RAY CRYSTALLOGRAPHY (3.3 ANGSTROMS).

MEDLINE=98455071;PubMed=9783750 [NCBI, ExPASy, EBI, Israel, Japan]

Lacy D.B., Tepp W., Cohen A.C., Dasgupta B.R., Stevens R.C.;

"Crystal structure of botulinum neurotoxin type A and implications for toxicity.";

Nat. Struct. Biol. 5:898-902(1998).

**Comments**

- **FUNCTION:** Inhibits acetylcholine release. The botulinum toxin binds with high affinity to peripheral neuronal presynaptic membrane, is then internalized by receptor-mediated endocytosis. The C-terminus of the heavy chain (H) is responsible for the adherence of the toxin to the cell surface while the N-terminus mediates transport of the light chain from the endocytic vesicle to the cytosol. After translocation, the light chain (L) hydrolyzes the 197-Gln-|-Arg-198 bond in SNAP-25, thereby blocking neurotransmitter release. Inhibition of acetylcholine release results in flaccid paralysis, with frequent heart or respiratory failure.
- **CATALYTIC ACTIVITY:** Limited hydrolysis of proteins of the neuroexocytosis apparatus, synaptobrevins, SNAP25 or syntaxin. No detected action on small molecule substrates.



- **COFACTOR**: Binds 1 zinc ion per subunit.
- **SUBUNIT**: Disulfide-linked heterodimer of a light chain (L) and a heavy chain (H).
- **SUBCELLULAR LOCATION**: Secreted.
- **PHARMACEUTICAL**: Available under the name BOTOX (Allergan) for the treatment of strabismus and blepharospasm associated with dystonia and cervical dystonia. Also used for the treatment of hemifacial spasm and a number of other neurological disorders characterized by abnormal muscle contraction.
- **MISCELLANEOUS**: There are seven antigenically distinct forms of botulinum neurotoxin: Types A, B, C1, D, E, F, and G.
- **SIMILARITY**: Belongs to the peptidase M27 family [view classification].
- **DATABASE**: NAME=BOTOX product information Web site; WWW="http://www.botox.com/site/".
- **DATABASE**: NAME=Protein Spotlight; NOTE=Issue 19 of February 2002; WWW="http://www.expasy.org/spotlight/back\_issues/sptlt019.shtml".

### Copyright

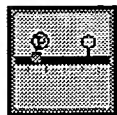
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### Cross-references

EMBL	X52066; CAA36289.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence] M30196; AAA23262.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence] X92973; CAA63551.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence] D67030; BAA11051.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence] M27892; AAA23269.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
PIR	A35294; BTCLAB.
PDB	3BTA; X-ray; A=1-1295.[ExPASy / RCSB / EBI]
MEROPS	M27.002; -. IPR008985; ConA_like_lect_gl. IPR011065; Kunitz_like.
InterPro	IPR006025; Pept_M_Zn_BS. IPR000395; Peptidase_M27. Graphical view of domain structure.
Pfam	PF01742; Peptidase_M27; 1. Pfam graphical view of domain structure.
PRINTS	PR00760; BONTOTOXILYSIN.
ProDom	PD001963; Botulinum; 1. [Domain structure / List of seq. sharing at least 1 domain]
PROSITE	PS00142; ZINC_PROTEASE; 1.
HOBACGEN	[Family / Alignment / Tree]
BLOCKS	P10845.
ProtoNet	P10845.
ProtoMap	P10845.
PRESAGE	P10845.
DIP	P10845.
ModBase	P10845.
SMR	P10845; 858342F754862579.
SWISS-2DPAGE	Get region on 2D PAGE.
UniRef	View cluster of proteins with at least 50% / 90% identity.

**3D-structure; Direct protein sequencing; Hydrolase; Metalloprotease; Neurotoxin; Pharmaceutical; Transmembrane; Zinc.**

### Features



Feature table viewer



Feature aligner

Key	From	To	Length	Description
INIT_MET	0	0		
CHAIN	1	447	447	Botulinum neurotoxin A light-chain.
CHAIN	448	1295	848	Botulinum neurotoxin A heavy-chain.
METAL	222	222		Zinc (catalytic).
ACT_SITE	223	223		
METAL	226	226		Zinc (catalytic).
METAL	261	261		Zinc (catalytic).
DISULFID	429	453		Interchain.
DISULFID	1234	1279		
TRANSMEM	626	646	21	Potential.
TRANSMEM	655	675	21	Potential.
VARIANT	26	26	1	V -> A.
MUTAGEN	261	261		E->A: Drastic decrease in enzymatic activity.
MUTAGEN	265	265		F->A: Decreases enzymatic activity.
MUTAGEN	365	365		Y->A: Decreases enzymatic activity.
CONFLICT	1	1		P -> Q (in Ref. 1).
CONFLICT	479	479		E -> P (in Ref. 9).
CONFLICT	875	875		T -> L (in Ref. 8).
CONFLICT	891	891		S -> K (in Ref. 8).
CONFLICT	1217	1217		S -> Y (in Ref. 11).
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STRAND	18	22	5	
STRAND	25	25	1	
STRAND	32	38	7	
TURN	39	40	2	
STRAND	41	47	7	
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TURN	74	77	4	
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TURN	99	99	1	
HELIX	101	112	12	
TURN	119	120	2	
TURN	123	124	2	
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STRAND	632	632	1
HELIX	634	636	3
TURN	637	643	7
HELIX	651	658	8
HELIX	660	663	4
STRAND	678	680	3
TURN	684	685	2
HELIX	687	719	33
TURN	720	720	1
HELIX	721	741	21
TURN	742	744	3
HELIX	745	750	6
TURN	751	752	2
TURN	757	758	2
HELIX	765	798	34
TURN	799	799	1
HELIX	800	823	24
TURN	824	828	5
HELIX	830	832	3
TURN	833	834	2
HELIX	835	843	9
TURN	844	845	2
HELIX	852	854	3
HELIX	859	870	12
HELIX	872	875	4
STRAND	878	883	6
TURN	884	885	2

STRAND	886	889	4
TURN	890	891	2
STRAND	894	899	6
STRAND	904	905	2
TURN	910	911	2
STRAND	912	916	5
TURN	919	920	2
STRAND	923	927	5
TURN	930	931	2
HELIX	934	937	4
STRAND	940	947	8
TURN	955	958	4
STRAND	960	965	6
STRAND	974	978	5
STRAND	981	987	7
TURN	989	990	2
STRAND	993	999	7
TURN	1010	1011	2
STRAND	1013	1020	8
TURN	1022	1023	2
STRAND	1025	1030	6
TURN	1031	1032	2
STRAND	1033	1039	7
TURN	1041	1042	2
STRAND	1051	1057	7
TURN	1062	1063	2
STRAND	1065	1074	10
HELIX	1080	1089	10
TURN	1090	1091	2
TURN	1093	1094	2
STRAND	1095	1095	1
STRAND	1097	1097	1
TURN	1099	1100	2
STRAND	1103	1103	1
STRAND	1105	1105	1
STRAND	1110	1112	3
TURN	1118	1119	2
STRAND	1121	1124	4
TURN	1129	1130	2
STRAND	1133	1136	4
STRAND	1141	1141	1
STRAND	1151	1151	1
STRAND	1158	1162	5
STRAND	1172	1172	1
STRAND	1174	1174	1
TURN	1175	1176	2
STRAND	1178	1185	8
TURN	1186	1187	2

STRAND	1188	1194	7
TURN	1196	1197	2
STRAND	1206	1208	3
TURN	1210	1212	3
TURN	1214	1215	2
STRAND	1217	1217	1
STRAND	1220	1222	3
STRAND	1225	1225	1
TURN	1227	1228	2
STRAND	1231	1231	1
STRAND	1234	1234	1
STRAND	1236	1238	3
TURN	1241	1242	2
STRAND	1247	1252	6
STRAND	1259	1263	5
HELIX	1264	1269	6
TURN	1270	1271	2
TURN	1278	1279	2
STRAND	1280	1280	1
STRAND	1283	1284	2
TURN	1288	1289	2

**Sequence information**

Length: **1295 AA** [This is the length of the unprocessed precursor]

Molecular weight: **149323 Da** [This is the MW of the unprocessed precursor]

CRC64: **858342F754862579** [This is a checksum on the sequence]

<u>10</u>	<u>20</u>	<u>30</u>	<u>40</u>	<u>50</u>	<u>60</u>
PFVNKQFNYK	DPVNGVDIAY	IKIPNVGQMQ	PVKAFKIHNK	IWVIPERDTF	TNPEEGDLNP
<u>70</u>	<u>80</u>	<u>90</u>	<u>100</u>	<u>110</u>	<u>120</u>
PPEAKQVPVS	YYDSTYLSTD	NEKDNYLKGV	TKLFERIYST	DLGRMLLSI	VRGIPFWGGS
<u>130</u>	<u>140</u>	<u>150</u>	<u>160</u>	<u>170</u>	<u>180</u>
TIDTELKVID	TNCINVIQPD	GSYRSEELNL	VIIGPSADII	QFECKSFGHE	VLNLTRNGYG
<u>190</u>	<u>200</u>	<u>210</u>	<u>220</u>	<u>230</u>	<u>240</u>
STQYIRFSPD	FTFGFEESLE	VDTNPLLGGAG	KFATDPAVTL	AHELIHAGHR	LYGIAINPNR
<u>250</u>	<u>260</u>	<u>270</u>	<u>280</u>	<u>290</u>	<u>300</u>
VFKVNTNAYY	EMSGLEVSFE	ELRTFGGHDA	KFIDSLQENE	FRLYYYNKFK	DIASLTNKA
<u>310</u>	<u>320</u>	<u>330</u>	<u>340</u>	<u>350</u>	<u>360</u>
SIVGTTASLQ	YMKNVFKEY	LLSEDTSGKF	SVDKLFKFDKL	YKMLTEIYTE	DNFVKFFKVL
<u>370</u>	<u>380</u>	<u>390</u>	<u>400</u>	<u>410</u>	<u>420</u>
NRKTYLNFDK	AVFKINIVPK	VNYTIYDGFN	LRNTNLAANF	NGQNTTEINM	NFTKLKNFTG
<u>430</u>	<u>440</u>	<u>450</u>	<u>460</u>	<u>470</u>	<u>480</u>
LFEFYKLLCV	RGIITSKTKS	LDKGYNKALN	DLCIKVNNWD	LFFSPSEDNF	TNDLNKGEEI
<u>490</u>	<u>500</u>	<u>510</u>	<u>520</u>	<u>530</u>	<u>540</u>
TSDTNIEAAE	ENISLDLIQQ	YYLTFNFDNE	PENISIENLS	SDIIGQLELM	PNIERFPNGK
<u>550</u>	<u>560</u>	<u>570</u>	<u>580</u>	<u>590</u>	<u>600</u>

```

KYELDKYTMF HYLRAQEFEH GKSRIALTNS VNEALLNPSR VYTFSSDYV KKVNKATEAA
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MFLGWVEQLV YDFTDETSEV STTDKIADIT IIIPYIGPAL NIGNMLYKDD FVGALIFSGA
      670      680      690      700      710      720
VILLEFIPEI AIPVLGTFAL VSYIANKVLV VQTIDNALS RNEKWDEVYK YIVTNWLAKV
      730      740      750      760      770      780
NTQIDLIRKK MKEALENQAE ATKAIINYQY NQYTEEEKNN INFNIDDLSS KLNESINKAM
      790      800      810      820      830      840
ININKFLNQC SVSYLMNSMI PYGVKRLEDF DASLKDALLK YIIDNRGTLI GQVDRCLKDKV
      850      860      870      880      890      900
NNTLSTDIPF QLSKYVDNQR LLSTFTEYIK NIINTSILNL RYESNHLIDL SRYASKINIG
      910      920      930      940      950      960
SKVNFDPIDK NQIQLFNLES SKIEVILKNA IVYNSMYENF STSFWIRIPK YFNSISLNNE
      970      980      990      1000     1010     1020
YTIINCMENN SGWKVSLNYG EIIWTLQDTQ EIKQRVVFKY SQMINISDYI NRWIFVTITN
      1030     1040     1050     1060     1070     1080
NRLNNSKIYI NGRLIDQKPI SNLGNIHASN NIMFKLDGCR DTHRYIWIKY FNLFDKELNE
      1090     1100     1110     1120     1130     1140
KEIKDLYDNQ SNSGILKDFW GDYLQYDKPY YMLNLYDPNK YVDVNNVGIR GYMYLKGRG
      1150     1160     1170     1180     1190     1200
SVMTTNIYLN SSLYRGTKFI IKKYASGNKD NIVRNNDRVY INVVVKNKEY RLATNASQAG
      1210     1220     1230     1240     1250     1260
VEKILSALEI PDVGNSQVV VMKSKNDQGI TNKCKMNLQD NNGNDIGFIG FHQFNNAI KL
      1270     1280     1290
VASNWNRYQI ERSRSLGCS WEFIPVDDGW GERPL

```

P10845 in FASTA  
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BLAST

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Compute pI/Mw, PeptideMass, PeptideCutter,  
Dotlet (Java)



ScanProsite, MotifScan



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## View of

## TrEMBL:

## Q84GJ4

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### Entry information

Entry name	<b>Q84GJ4_CLOBO</b>
Primary accession number	<b>Q84GJ4</b>
Secondary accession numbers	None
Entered in TrEMBL in	Release 24, June 2003
Sequence was last modified in	Release 24, June 2003
Annotations were last modified in	Release 26, March 2004

### Name and origin of the protein

Protein name	<b>Neurotoxin type A light chain [Fragment]</b>
Synonyms	None
Gene name	None
From	Clostridium botulinum [TaxID: 1491]
Taxonomy	Bacteria; Firmicutes; Clostridia; Clostridiales; Clostridiaceae; Clostridium.

### References

- [1] NUCLEOTIDE SEQUENCE.  
Seong H.Y., Kim J.S., Lee M.H., Choi Y.M., Choi S.-Y.;  
Submitted (OCT-2002) to the EMBL/GenBank/DDBJ databases.

### Comments

None

### Cross-references

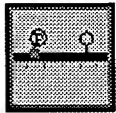
EMBL	AY166872; AAO21363.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
HSSP	P10845; 3BTA. [HSSP ENTRY / PDB]
	GO:0008233; Molecular function: peptidase activity ( <i>inferred from electronic annotation</i> ).
	GO:0009405; Biological process: pathogenesis ( <i>inferred from electronic annotation</i> ).
GO	GO:0006508; Biological process: proteolysis and peptidolysis ( <i>inferred from electronic annotation</i> ).
	QuickGo view.
	IPR011591; Botulinum.



InterPro IPR000395; Peptidase\_M27.  
 IPR006025; Pept\_M\_Zn\_BS.  
 Graphical view of domain structure.  
 Pfam PF01742; Peptidase\_M27; 1.  
 Pfam graphical view of domain structure.  
 PRINTS PR00760; BONTOXILYSIN.  
 ProDom PD001963; Botulinum; 1.  
 [Domain structure / List of seq. sharing at least 1 domain]  
 PROSITE PS00142; ZINC\_PROTEASE; UNKNOWN\_1.  
 HOBACGEN [Family / Alignment / Tree]  
 ProtoMap Q84GJ4.  
 PRESAGE Q84GJ4.  
 ModBase Q84GJ4.  
 SMR Q84GJ4; 89C98D162AC9FDBE.  
 SWISS-2DPAGE Get region on 2D PAGE.  
 UniRef View cluster of proteins with at least 50% / 90% identity.

**Keywords**

Neurotoxin; Toxin.

**Features**

Feature table viewer

Key	From	To	Length	Description
NON_TER	448	448		

**Sequence information**

Length: 448 AA [This is the Molecular weight: 51325 Da  
 length of the partial [This is the MW of the partial  
 sequence] sequence]

CRC64: 89C98D162AC9FDBE [This is  
 a checksum on the sequence]

10	20	30	40	50	60
MPFVNKQFNY	KDPVNGVDIA	YIKIPNAGQM	QVKAFKIHNK	IWVIPERDTF	TNPEEGDLNP
70	80	90	100	110	120
PPEAKQVPVS	YYDSTYLSTD	NEKDNYLKGV	TKLFERIYST	DLGRMLLTSI	VRGIPFWGGS
130	140	150	160	170	180
TIDTELKVID	TNCINVIQPD	GSYRSEELNL	VIIGPSADII	QFECKSFGHE	VLNLTRNGYG
190	200	210	220	230	240
STQYIRFSPD	FTFGFEESLE	VDTNPLLGA	KFATDPAVTL	AHELIHAGHR	LYGIAINPNR
250	260	270	280	290	300
VFKVNTNAYY	EMSGLEVSFE	ELRTFGGHDA	KFIDSLQENE	FRLYYYNKF	DIASLTNKA
310	320	330	340	350	360
SIVGTTASLQ	YMKNVFKEY	LLSEDTSKGF	SVDKLKFDKL	YKMKTEIYTE	DDNFVKFFKV
370	380	390	400	410	420
LNRKTYLNF	KAVFKINIVP	KVNYTIYDGF	NLRNTNLAAN	FNGQNTINN	MNFTKLKNFT

430 440  
GLFEFYKLLC VRGIITSKTK SLDEGYNK

Q84GJ4 in FASTA  
format

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*Request for annotation of this TrEMBL entry*

**BLAST**

BLAST submission on  
ExPASy/SIB  
or at NCBI (USA)





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Dotlet (Java)



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## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US97/15394

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : Please See Extra Sheet.

US CL : Please See Extra Sheet.

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/184.1, 192.1, 247.1; 435/69.1, 69.7, 325, 320.1; 530/388.4, 389.5

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

MEDLINE, BIOSIS, WPIDS, CAPLUS, APS

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	THOMPSON et al. The Complete Amino Acid Sequence of the Clostridium botulinum Type A Neurotoxin, Deduced by Nucleotide Sequence Analysis of the Encoding Gene. Eur. J. Biochem. April 1990, Vol. 189, pages 73-81, see entire document.	1-24
Y	BINZ et al. The Complete Sequence of Botulinum Neurotoxin Type A and Comparison with Other Clostridial Neurotoxins. Journal of Biological Chemistry. June 1990, Vol. 265, No. 16, pages 9153-9158, see entire document.	1-24
Y	ROITT. Essential Immunology. Oxford: Blackwell Scientific Publications. 1988, especially pages 173-178.	1-24

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*A* document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
*E* earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
*L* document which may throw doubt on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*A* document member of the same patent family
*O* document referring to an oral disclosure, use, exhibition or other means	
*P* document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

10 OCTOBER 1997

Date of mailing of the international search report

23 DEC 1997

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

EVELYN RABIN

Telephone No. (703) 308-0196

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US97/15394

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SIEGEL. Human Immune Response to Botulinum Pentavalent (ABCDE) Toxoid Determined by a Neutralization Test and by an Enzyme-Linked Immunosorbent Assay. Journal of Clinical Microbiology. November 1988, Vol. 26, pages 2351-2356, see entire document.	1-24
Y	FORD et al. Fusion Tails for the Recovery and Purification of Recombinant Proteins. Protein Expression Purification. 1991, Vol. 2, pages 95-107, see entire document.	1-24
Y	LECLERC et al. Induction of Virus-Neutralizing Antibodies by Bacteria Expressing the C3 Poliovirus Epitope in the Periplasm. Journal of Immunology. April 1990, Vol. 144, pages 3174-3182, see entire document.	1-24
Y	KLEID. Using Genetically Engineered Bacteria for Vaccine Production. Annals New York Acad. Sci. 1983, Vol. 483, pages 23-30, see entire document.	1-24

Form PCT/ISA/210 (continuation of second sheet)(July 1992)\*

**INTERNATIONAL SEARCH REPORT**

International application No.  
PCT/US97/15394

**A. CLASSIFICATION OF SUBJECT MATTER:**  
IPC (6):

A61K 39/00, 39/38, 38/08; C12P 21/06, 21/04, 21/08; C12N 15/00, 15/09, 15/63, 15/70, 15/74; C07K 16/00

**A. CLASSIFICATION OF SUBJECT MATTER:**  
US CL :

424/184.1, 192.1, 247.1; 435/69.1, . 69.7, 325, 320.1; 530/388.4, 389.5